Long-term trends of use of health service among heart failure patients

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Running title: Long-term readmission rates in heart failure patients
Abstract

Aims

We aimed to identify subgroups in the patient population with different trajectories of long-term readmission rates. The study also aimed to assess common causes and their sequences of readmissions for each subgroup.

Methods

Patients with a primary diagnosis of heart failure (HF) in the period 2008-2009 were identified using nationally representative primary care data linked to national hospital data, which contain information on 10.5 million patients. HF patients were followed up for 5 years. Group-based trajectory models and sequence analysis were applied.

Results

The model categorised the HF population (n=9466) into 5 subgroups: low-impact (66.9%); two intermediate ones (27.4%); chronic high-impact (2.3%) with steady high annual readmission rates; and short-term high-impact (3.4%) with rapid decline in readmission rates. The groups were defined by their trends of yearly number of readmissions. The all-cause 5-year mortality was highest in the short-term high-impact group (n=185, 72.8%), followed by group 2 (intermediate users) (n=744, 58.8%), low-impact (n=4244, 56.9%), chronic high-impact (n=88, 37.6%) and group 1 (intermediate users) (n=401, 30.3%) (p < 0.01). Compared with low-impact users, high-impact users were associated with higher mortality, bereavement episodes, and more out-of-hours GP visits. The chronic high-impact users had distinct sequences of causes of emergency admissions most often consisting of chest infection, ischaemic heart disease, and cardio-pulmonary signs and/or symptoms.
Conclusion

Chronic high-impact users constitute a small proportion of total patients, but they have increasingly high use of healthcare services. Short-term high-impact users represent largely end of life patients. They require prompt involvement of the palliative care team to reduce unnecessary readmissions to hospital.

Keywords

Readmissions, trajectory analysis, sequence analysis, healthcare visits
Introduction

Many patients suffering from HF undergo multiple hospital admissions, and the readmission rate in the first 6 months can be as high as 45%. (1,2,3) Those with higher readmission rates have been termed high-impact users, sometimes defined as three or more emergency admissions within a year. (4) To improve their clinical viability, programs to reduce readmission rate should be targeted at high-impact users. (5)

The identification of high-impact users has been challenging. (6) Previous risk models to predict readmissions had various limitations. (7) They were developed on RCT populations and so were not representative of general patients with HF due to selection bias. Further, the impact of various social factors on the readmission rate has largely not been assessed, and most studies have merely evaluated the basic demographics like age, sex, ethnicity and socio-economic status. (8) Previous models were derived to predict short-term risk of a single event (e.g. readmission or death within 30 days to 1 year) only and do not distinguish between patients with a set of readmissions at the end of life or other short-term crisis – in whom the rate soon returns to zero or near zero – and those whose high readmission rate is sustained, in part due to suboptimal management in hospital or in primary care. (9)

An important unanswered question is whether the long-term high-impact users have distinct chronological causes of emergency readmissions compared with the other groups. (10) This is necessary to investigate the series of physiological processes leading to a decline in the health status of the high-risk patients and assess whether this chain can be prevented by simple measures in the community. In medicine, the sequence of events has an influence on prognosis. (11) For example, the diagnosis of heart failure following atrial fibrillation is associated with a higher mortality compared with diagnosis of atrial fibrillation after heart
failure. So far, we do not have any information on whether the causes and their sequences for readmissions differ in the subgroups of HF patients.

To our knowledge, this study is the first attempt to go beyond binary categories and classify HF patients into subgroups and identify high-impact users based on the long-term readmission rate. The study will also aim to understand the characteristics of high-impact users and the predictors associated with them. This will help us understand the common causes (primary diagnoses) of emergency readmissions and their distinct sequences in high-impact users in particular, with the aim of identifying common preventable chains of events to reduce readmission rates.
Methods

Databases

Data were obtained from Clinical Practice Research Datalink (CPRD) linked to Hospital Episode Statistics (HES) and Office for National Statistics (ONS) deaths database. CPRD is a large national primary care database with over 13 million enrolled patient medical records across the country and contains 8.5% of the patient population in England. It includes information on demographics, referrals, tests, investigations, prescriptions, and medical diagnosis and procedural information for each consultation with the general practitioner (GP). Around 660 practices have volunteered in CRPD to share patient data. Half of the general practices associated with CPRD are linked to HES data (non-English practices are not linked to HES, as other UK countries have their own HES-type databases that are not included in CPRD). Moreover, 95% of the HES data is linked to ONS data. HES is the warehouse of patient administrative data covering all in-patient and day case stays in public National Hospital Service (NHS) hospitals in the country as well as information on private patients treated in these hospitals. All diagnoses are recorded using ICD-10 (International Classification of Diseases), whilst the Office of Population, Census and Survey version 4.7 (OPCS 4.7) coding is used for procedures. The fact and date of death are obtained from ONS (Office for National Statistics). The primary conditions in ICD are well coded but it does not provide detailed information on the subtype of the diagnoses, such as, type of chronic renal failure or respiratory conditions. This is a particular limitation of the use of administrative data.

Patients

Patients over the age of 18 with the first-time diagnosis of heart failure recorded between 1st Apr 2008 and 31st March 2009 who were identified through linked data were included in the study if they contributed to CPRD and allowed linkage to the other datasets. Medical codes
recorded by GPs (“medcodes”) were used to identify patients who were first documented to have heart failure in the community (Appendix I); the ICD-10 code I50X was used to identify patients who were diagnosed with HF in hospital. Earlier studies have shown that most of the diagnoses are well recorded in CPRD data by the General Practice staff.(12) All the patients were traced back 5 years to verify the absence of any earlier HF diagnosis, and to retrieve data on their past medical history, social and management-related factors. Patients were followed up within the database for five years up to March 2014.

**Statistical methods**

Group-based trajectory modelling (GBTM) based on zero-inflated Poisson analysis was used to categorise patients into subgroups and to predict development of their trajectory pathways.(15) In order to determine the optimum number of the subgroups within a population, the best model was chosen based on the following criteria: smallest value of Bayesian Information Criteria (BIC), smallest value of Akaike Information Criteria (AIC), each trajectory with significant parameter estimates (p<0.05), minimal 95% confidence interval, a higher value for average posterior probability (>0.70) for each subgroup, and a higher value (>5.0) for odds of correct classification (OCC).(15) The effect of covariates on the probability of belonging to the subgroup was modelled with multinomial logistic regression. The group with the lowest persistent readmission rate was labelled as ‘low-impact users’ and used as a reference group in the regression. ANOVA analysis was used to the difference between the outcomes of 2 or more groups.

Risk factors were identified from previous studies. The patient-based factors were age at diagnosis, sex, and past medical history recorded in the last 5 years preceding the diagnosis of HF. Age was grouped into categories 18-45, 45-54, 55-64, 65-74, 75-84, and 85+. (10) The social and lifestyle factors included bereavement, marital or relationship problems
(separation, break-up, divorce, or cheating on a partner), history of smoking and heavy alcohol intake, previously found to correlate with the prognosis of heart failure.\(^8\) For smokers, we distinguished between current and former. Bereavement was defined as loss of any immediate family member. The management-based factors consisted of GP visits coded for monitoring of renal function, flu vaccination, measurement of blood pressure and exercise recommendation. Other factors included 3 or more emergency admissions for any reason vs. <2 admissions in the year preceding the diagnosis of HF \(^{16}\), annual GP visits (including out-of-hours) and out-of-hours GP visits in the year preceding the diagnosis of HF. Previous annual GP visits and annual out-of-hours GP visits did not have linear relationships with the high-impact users. Hence, they were categorised according to percentile ranges (<25\(^{th}\), 26-50\(^{th}\), 51-75\(^{th}\) and >75\(^{th}\) percentiles). The effect of HF diagnosed as an inpatient and history of use of medications for treatment of signs and symptoms of HF was also evaluated.

Medication use for the management of signs and symptoms of heart failure included prescriptions for drugs like loop and thiazide diuretics, beta-blockers, angiotensin-converting-enzyme inhibitors, angiotensin II receptor antagonists, digoxin, and bumetanide.\(^{17}\) The information on the social factors and management-based factors was obtained for the 5 years before the date of diagnosis of HF. The medcodes for social/lifestyle and management factors are listed in Appendix I.

For validation of the identified high-impact user and significant predictors associated with them, the model was applied to a different cohort of HF patients who were diagnosed during the financial year from 1\(^{st}\) April 2007 to 31\(^{st}\) March 2008.

The sequence analysis was conducted using TraMineR package (version 1.8-12) in R language statistical software.\(^{18}\)

Results
The model categorised the HF population (n=9466) into 5 subgroups, according to readmission rates: low-impact group, 2 intermediate groups, short-term high-impact and chronic high-impact groups (Figure 1). Group 1 (66.5%) was considered low-impact group because it had persistently low readmission rates. Group 2 (14.5%) and Group 3 (12.9%) had intermediate use of hospital care. Group 2 showed constant intermediate readmission rates, whereas Group 3 started with a moderate annual readmission rate that steadily declined. Group 4 and 5 had the highest readmission rate and were labelled as high-impact users. Group 4 (3.4%) were termed as short-term high-impact because they had a rapid drop in the annual readmission rate after a very high readmission rate in their first year of follow-up. Group 5 (2.3%) were labelled as chronic high-impact, with a relatively steady high readmission rate with only a gradual decline during the follow-up period. The sensitivity and specificity of the model to detect chronic high-impact users was 81.3% and 98.8%, respectively. When the significant predictors associated with high-impact users were applied to the validation cohort of patients, the c statistic was 0.87. The risk factors associated with the high-impact users, Group 4 and 5, are given in Table 1 and 2.

Overall, 9466 patients had a first-time diagnosis of heart failure in 2008-9. The mean age was 76.2 (SD 14.3) and 4836 (51.1%) were women. 73.8% (n=6993) were diagnosed with heart failure as an inpatient in the hospital, and over half (n=5833, 61.6%) presented with signs and symptoms of heart failure in the community. Commonly recorded pre-diagnosis comorbidities were hypertension (n=4494, 33.5%), ischaemic heart disease (n=3477, 36.7%), atrial fibrillation (n=3174, 33.5%), diabetes (n=1570, 16.5%), cardiac valvular disease (n=1392, 14.7%), acute myocardial infarction (n=1338, 14.1%), stroke (n=1212, 12.8%), dementia (n=908, 9.6%), obesity (n=672, 7.1%), peripheral vascular disease (n=586, 6.2%), and myocarditis/cardiomyopathy (n=303, 3.2%).
The overall 5-year mortality was 53.8% (n=5662). The all-cause 5-year mortality was highest in the short-term high-impact group (n=185, 72.8%), followed by group 2 (intermediate users) (n=744, 58.8%), low-impact (n=4244, 56.9%), chronic high-impact (n=88, 37.6%) and group 1 (intermediate users) (n=401, 30.3%) (p < 0.01). Various outcomes for each group during the follow-up period are shown in Table 3. The trajectories of out-of-hours GP visits among subgroups of HF patients are shown in Figure 2.

Common causes of emergency admissions after the diagnosis of HF were heart failure (n=1896 [21.5%]), chest infection (n=1293 [14.7%]), myocardial infarction (n=658 [7.5%]), external injuries (n=442 [5.0%]), and atrial fibrillation (n=434 [4.9%]). The most common causes of admissions in all subgroups were heart failure, chest infection and myocardial infarction. Short-term high-impact users had more admissions for cardio-respiratory signs and symptoms and ischaemic stroke (Table 4).

The lasagne plot displays chronological order of healthcare service use by each group (Figure 3). Each type of service use was colour coded. Similarly, the plot in Figure 4 shows cumulative frequencies of type of healthcare services used following first time diagnosis of HF. As noted earlier, chronic high-impact users had high readmission rates and short-term high-impact users had high mortality. The common sequences of the types of healthcare visits among short-term high-impact users were predominantly emergency hospital admissions resulting in death. The number of consecutive hospital admissions, elective and emergency, was more common in chronic high-impact users. The frequency of transition from emergency GP visit to emergency hospital admission was higher among intermediate and high-impact users than with low-impact users. 82.9% and 81.2% of the chronic high-impact users had elective hospital admission followed by emergency admission and vice versa, respectively. This was in contrast to 29.9% and 25.5% among low-impact users, respectively. Similarly,
Emergency GP visit followed by emergency hospital admission occurred in 40.2% of the chronic high-impact users, whereas, only 13.4% of the low-impact users had it.
Discussion

Based on annual readmission rates during a five-year period, we divided patients into 5 subgroups, among which we importantly distinguished between chronic and short-term high-impact users. Certain risk factors were strongly associated with all high-impact users, such as having a first-time diagnosis of HF as an inpatient in a hospital, older age and background of stroke, anaemia, myocardial infarction, atrial fibrillation, respiratory disease, and hypertension. During the follow-up period, the proportion of visits for bereavement episodes, relationship difficulties, and out-of-hours GP visits were significantly higher in high-impact users. They had a distinct set of sequences of emergency readmissions consisting mainly of cardio-pulmonary conditions. Short-term high-impact users had similar sequences of readmissions to those of chronic high-impact users but they had a higher mortality rate. These were the patients at the end of life pathway.

The common causes of readmissions among high-impact users among HF were similar to those found in previous studies.(19,20) During 18 months’ follow-up, one-third of the HF patients had readmissions due to HF-related complications, another one-third were due to other cardio-vascular conditions, and the rest of the readmissions were due to non-cardiovascular conditions. However, our analysis goes beyond studies of single readmissions and found that the high-impact users had distinct sub-sequences of causes of readmissions, mainly respiratory tract infections, cardio-pulmonary signs and symptoms, and ischaemic heart disease.

Patient management might be improved with simple clinical tactics. Disease management programs that have been shown to reduce overall and HF-related readmission rates in patients with different age groups and severity of HF can be targeted to chronic high-impact users to save resources.(21,22) Enrolment of high-risk patients in pro-active management programs...
has been shown to reduce hospitalisation costs and improve quality of life in HF patients. (23) We found that the high-impact users had higher incidence of bereavement and relationship difficulties, which may have led to delays in seeking help for their medical condition. (23) These patients may get benefit from social services and regular primary care review to help them deal with problems in their personal life. Furthermore, those patients with multiple readmissions were mainly readmitted for selected conditions which can potentially be prevented in the community via interventions such as regular GP review, for secondary prevention of ischaemic heart disease and to prevent acute onset of HF with exercise recommendations, and compliance with HF medications. (24, 25) The new guidelines in the management of heart failure patients have also suggested regular flu vaccination as a part of lifestyle recommendations. (24)

In the light of this study, two policy changes can likely improve the care of HF patients. The corresponding out-of-hours GP visits among subgroups match the trends in readmission rate, indicating that these patients repeatedly call for help in the community during out-of-hours. When the GP attends them, given their history of HF, they have a low threshold to refer them to hospital care. (26) Recent point-of-care devices have been developed for prompt measurement of troponin and inflammatory markers. (27) Further research is required to assess if these devices can make decision making process easier for the GPs if they encounter a patient with cardio-pulmonary signs or symptoms. Secondly, most of these patients have multiple co-morbidities requiring X-rays and blood tests before treating them. It may be that direct contact between cardio-vascular patients and the medical team in the hospital is required in case if they become unwell. This way the investigations are carried out in a shorter time span and treatment is started early.

Certain factors have to be considered before interpreting the results from this study. Primary care data is obtained from 674 practices in the UK which are registered with CPRD. It is one
of the largest linked primary care databases in the world, which provides a great opportunity to assess various hospital- and primary care-based factors as well as to evaluate long-term outcomes. Patients included in the CPRD data are representative of the UK population by age, sex and ethnic group.(28) CPRD is increasingly being used and has been validated for research in heart diseases.(29) The incorporation of the information from both primary and secondary care added predictive power to the model. One common problem with administrative but also many clinical databases is that some fields are prone to error,(30) but the coding has been shown to be sensitive and accurate in identifying the patient cohort and establishing the primary diagnosis.(12) Also, the study has only included readmission rate as an outcome as the focus of the study was to understand long-term morbidity and real life events that impact quality of life. Further work could include other outcomes, such as outpatient clinic use, functional health, etc, although CPRD lacks quality of life measures. Whilst we attempted to assess all types of social events and their association with high-impact users, some social factors, e.g. patient was a carer or had a financial problem, were not commonly coded and were therefore not included in the statistical model.

In conclusion, high-impact users had distinct characteristics, patterns of readmission rate and sub-sequences of multiple readmissions. Chronic high-impact users were often not diagnosed in the community but later as an inpatient in the hospital. The challenge for the health service is to identify these patients early in the community and start them promptly on a HF management pathway that includes frequent review of their co-morbidities related to cardiopulmonary conditions. Early involvement of social services can improve care of these patients by providing holistic management and dealing with social and lifestyle issues. Our trajectory model could be used to identify short-term high-impact users who are terminally ill. Involvement of the palliative care community team will help avoid unnecessary hospital admissions and improve quality of life.
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Conflict of interest

Dr. Aylin reports grants from Dr Foster (Owned by Telstra), during the conduct of the study. Other authors declare no conflict of interest.

Declaration of Helsinki

The study complies with the Declaration of Helsinki, that the locally appointed ethics committee has approved the research protocol.
References


Figure Legends

Figure 1. Trajectories of subgroups among HF patients (dotted lines represent 95% confidence intervals).

Figure 2. Trajectory of mean out-of-hours GP visits in comparison to mean annual readmission rate among subgroups in HF.

Figure 3. The sequence of healthcare visits in different subgroups of HF patients in the follow-up period.

Figure 4. The proportion of type of healthcare visits during each consecutive health care use among subgroups of HF patients.

Table 1. Sociodemographic and past medical history associated with high-impact users compared with the low-impact users.

Table 2. Management related factors associated with high-impact users compared with the low-impact users.

Table 3. The incidence of healthcare use and social events in the subgroups during the follow-up period. (The cardiac imaging included chest x-ray, echocardiogram, cardiac angiogram, computed tomography and magnetic resonance imaging of the heart).

Table 4. Common distinct sequences of causes of readmissions associated with various subgroups in the patient population.
Appendix 1.

Diagnosis of heart failure:

'G58.00' 'G580.00' 'G580000' 'G580100' 'G580.11' 'G580.12' 'G580.13' 'G580.14' 'G580200'
'G580300' 'G580400' 'G581.00' 'G581000' 'G58.11' 'G581.11' 'G581.12' 'G581.13' 'G582.00'
'G583.00' 'G583.11' 'G584.00' 'G58z.00' 'G58z.11' 'G58z.12' 'G5yy900' 'G5yyA00'

Smoking:

Current smoking status:

'12958', '12944', '1878', '3568', '1822', '54', '12942', '12967', '31114', '12964', '30423', '46654',
'98347', '104310', '102361', '12953', '2111', '18211', '38112', '18926', '74907', '94958', '91708', '41042',

Status of ex-smoking:

'12961', '12957', '12955', '12956', '12959', '12946', '97210', '776', '99838', '60', '100495', '26470', '19488',
'90', '12878', '98447', '100963'

Heavy alcohol intake:

'322', '749', '956', '12985', '19495', '26472', '669', '1618', '7545', '7746', '8999', '12974', '12976', '12977',
'12982', '12983', '12984', '19401', '19493', '19494', '28150', '30695'

Renal function recorded at GP visit:

'32', '1097', '2072', '13812', '13813', '13814', '26832', '26943', '26944', '26945', '103493', '2998', '3980',
'4265', '5458', '10768', '25763', '26001', '37236');

Blood pressure monitoring at GP visit:

'1', '101', '57', '100', '5341', '27274', '859', '3481', '5020', '14643', '14452', '23312', '43547', '22595', '38278',
'27271', '31305', '14640', '29261', '14641', '41052', '14642', '48008', '27273', '25553', '19905', '37242',

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Medications used to treat signs and symptoms of HF:

Diuretics:

'10066','10316','10392','10422','10781','11265','11268','11348','11351','1143','1144','11448','11469','11487','11526','11561','11567','11641','11937','11965','11983','11987','12226','12294','12313','12318','12354','12367','12411','12412','12574','12815','12836','12858','12874','12937','1301','13026','13123','13435','1369','13755','13821','14228','14283','14387','14477','14478','14587','14738','14761','14837','14870','14943','14960','14965','14983','15031','15085','15096','15108','15121','1520','15341','15605','156487','15784','15874','15958','16060','16061','16196','16206','16212','16285','16371','16701','16708','16710','16924','17006','17120','17474','17545','17624','17633','17655','17686','17689','1776','1780','17960','1807','18096','18200','18202','18219','18223','18263','18269','18325','18332','18497','18650','18716','18903','18910','1904','19056','19192','19194','19198','19204','19208','19223','19258','193','19300','196','19690','20117','20188','20538','20579','20849','20975','21053','211','21162','21231','21423','21849','21938','21943','22439','22568','22708','23252','23456','23478','23642','24041','24268','24359','24482','24484','24632','24832','24835','2493','2495','25334','25382','25717','25965','25998','26292','26529','26995','27447','27520','27690','27696','2777','2772','27871','2788','27926','28127','28129','28438','28486','28586','28724','28725','28820','28902','29130','29530','2961','29634','2971','29780','2982','30039','3050','30625','3069','30773','30875','30913','30921','31072','31307','31548','31587','31716','31773','31810','31932','32002','3203','32048','32091','32166','3222','32241','32277','3248','32514','32560','32597','32857','3287','32896','32918','32934','33057','33078','33095',...
Angiotensin-Converting-Enzyme inhibitors (ACEi):

'1021', '10882', '10902', '11133', '11197', '1121', '11351', '1143', '1144', '11561', '11641', '11937', '11983',

'11987', '12313', '12411', '12412', '12574', '12815', '12858', '13026', '13589', '13755', '14228', '14387',

'14477', '14478', '147', '14960', '15031', '15085', '15096', '15108', '15121', '15135', '1520', '15605', '15958',

'16196', '16197', '16212', '16701', '16708', '16710', '16924', '17006', '17120', '17474', '17624', '17633',

'17655', '1807', '18219', '18263', '18269', '18325', '1904', '19198', '19204', '19208', '19223', '196', '19690',

'20188', '20579', '20849', '20975', '21053', '21162', '21231', '21943', '22439', '22708', '23252', '23478',

'23642', '24041', '24482', '25998', '26995', '277', '27871', '28127', '28486', '28586', '28724', '28725', '28820', '28902', '29130', '29530', '29627', '2982', '30039', '3069', '30921', '31307', '31587', '31716', '31810', '3203',

'32048', '32166', '32241', '32514', '32560', '32597', '32857', '32934', '33057', '33078', '33095', '3310',

'33336', '33353', '33646', '33811', '33894', '33977', '34357', '34382', '34390', '34400', '34412', '34429',

'34431', '34432', '34453', '34471', '34490', '34505', '34528', '34539', '34540', '34544', '34562', '34567',

'34583', '34589', '34651', '34652', '34657', '34696', '34698', '34710', '34712', '34719', '34732', '34768',

'34798', '34799', '34797', '34893', '34936', '34937', '34943', '34952', '34953', '35007', '35302', '35731',

'35794', '36742', '36753', '37080', '37087', '3720', '37655', '37770', '37777', '37908', '37930', '37964',

'37965', '37971', '37978', '38026', '38034', '38285', '38308', '3839', '38510', '38854', '38899', '38995',


24
Beta-blockers:

'1006' ,'10191' ,'10429' ,'1048' ,'1050' ,'10627' ,'10716' ,'10777' ,'10892' ,'1124' ,'11338' ,'11380' ,'11432' ,'11454' ,'11711' ,'11793' ,'12037' ,'12054' ,'12141' ,'12191' ,'12296' ,'12456' ,'12495' ,'12517' ,'12519' ,'12651' ,'12678' ,'12749' ,'1288' ,'1290' ,'1295' ,'13051' ,'1333' ,'1334' ,'13394' ,'13487' ,'13499' ,'13526' ,'13871' ,'14030' ,'14057' ,'14058' ,'14117' ,'14126' ,'14146' ,'14211' ,'14286' ,'14319' ,'14438' ,'1448' ,'14552' ,'14673' ,'14808' ,'14877' ,'14952' ,'15042' ,'15117' ,'15176' ,'15488' ,'15619' ,'1572' ,'15730' ,'1597' ,'16032' ,'16156' ,'16645' ,'16776' ,'1684' ,'17082' ,'17115' ,'17149' ,'17322' ,'17462' ,'17615' ,'17759' ,'17783' ,'1788' ,'18114' ,'18185' ,'18287' ,'18414' ,'18743' ,'18950' ,'18956' ,'19055' ,'1910' ,'19142' ,'19149' ,'19172' ,'19178' ,'19182' ,'19191' ,'19200' ,'19202' ,'19437' ,'197' ,'19853' ,'19858' ,'20012' ,'20015' ,'20082' ,'20093' ,'20363' ,'20468' ,'20502' ,'20728' ,'21025' ,'21133' ,'21182' ,'21506' ,'21508' ,'21838'.
Angiotensin II receptor blockers (ARB):

520, 529, 531, 575, 624, 764, 828, 1293, 1780, 2971, 3222, 4155, 4226, 4540, 4645, 4685, 4741, 4818, 5013, 5117, 5723, 5988, 6217, 6285, 6351, 6437, 6518, 6877, 6939, 7043, 7338, 9196, 9745, 10316, 10323, 11251, 11252, 11348, 11448, 11469, 11526, 11864, 12836, 12874, 13123, 13821, 14943, 14983, 16060, 16161, 16285, 16371, 17545, 17686, 17689, 18200, 18202, 18903, 18910, 20117, 21423, 23456, 24268, 24359, 24484, 24632, 25382, 27520, 29634, 31072, 35096, 35173, 35174, 35189, 35196, 35304, 35317, 35329, 35343, 35380, 35481, 35697, 35753, 37650, 37747, 38367, 38395, 38459, 38889, 39021, 39199, 39786, 39944, 39984, 40316, 40571, 40639, 40668, 40711, 41203, 41205, 41232, 43322, 43915, 44778, 45600, 46355, 46687, 46715, 46792, 47006, 47467, 47573, 47616, 47727, 48039, 48398, 49492, 49588, 50185, 50971, 51117, 51186, 51368, 51519, 51601, 51647, 51897, 52189, 52208, 52427, 52559, 52659, 52858, 52886, 52972, 53220, 53680, 53755, 53833, 54049, 54057, 54326, 54404, 54726, 54735, 54740, 54843, 55017, 55160, 55187, 55296, 55358, 55718, 55821, 56104, 56204, 56606, 56970, 56975, 57026, 57028, 57266, 57273, 57796, 57977, 58108, 58201, 58274, 58646, 58649, 58669, 58910, 58967, 59029, 59086, 59271, 59340, 59351, 59393, 59448, 59690, 59750, 59802, 60076, 60506, 60597, 61053, 61177, 61288, 61442, 61495, 61754, 61781, 62035, 62140, 62337, 62376, 62388, 62415, 62911, 63222, 63337, 63385, 63411, 63717, 63890, 63918, 64359, 64888, 65065, 65094, 65228, 65274
Digoxin:

'16366','17169','20844','20944','2302','24719','25043','2511','25238','27523','27547','29282','3181',
'3286','3308','33274','333','33612','33675','34017','34023','34024','34327','34328','34519',
'34948','36','3705','40245','42989','42990','43577','48587','54117','792','94','9522'

Bumetanide:

'12226','12294','14587','15341','1776','19300','2493','2495','2788','30913','31932','34613',
'34934','36767','39602','45305','5218','55548','6160','7806','814'

Marital/relationship problems:

Divorce:

'4204','27385','5055','4925','42428','1522','9910','838','2159','20217','20313'

Widow:

'4312'

Separation/break-up/cheating on partner:

'1349','29544','723','954','333','3551','1540','30950','15313','42321','54816','29543','22873','42454',
'3483','24055','15020','6104','4531','3111','4149','2830','4177','42383','21259','27432','1650','465',
'23514','464','7840','34771','23409','27434','56178','20536','23445','39651','15777','42400','21433',
'39879','21925','37551','21619','9112'

Exercise recommendation coded by GP:

'13083','13084','13085','29051','32840','53124','41879','57429','18483','36399','24871','18457',
'53166','18168','13087','36','26525','95900','19528','96647','42314','106298','26524','109818',
'35492','109915','26523','19529','26526','26528','26529','26521','48555','31588','35493','13086',
'26530','59258','45785','32844','96646','96374','96913','96213','97179','26527','3734','62183',
'52631','29056','67610','94051'
Bereavement episodes:
'400','11228','12303','207','87334','8218','9163','1516','1502','3749','3854','16844','29382','5622','31106','28440','11251','17802','25097','18119','10526'

History of flu vaccination:
'210','2694','23550','6','103324','94301','95092','107646','97941','105077','107413','107730','110219','110182','98217','108772','98306','98234','98302','98449','98303','98183','98184','98304','104688','105195','107297','107573','107352','107156','106994','106995'

Atypical signs and symptoms of heart failure:

Weight gain:
'19208','102856','6533'

Weight loss:
'4663','5812','102563','12398','37937','104002'

Cachexia:
'24068','36473','53801'

Cardiac murmur:
'291','3138','18916','21953','7661','12557','894','3910','157','19572','3982','30090','44516','23007','52770','4857','95082','59965','103653','103644','103619','22550'

Peripheral oedema:
'3158','6047','2140','102720','102627','30309','11396','1906','9392','22734','15047','5919','31377','9108','49411','6764','61224','19714','6651','18685','20553','1906','1284','7106','19358','6585','5155'

Lung crepitation:
'9062','15866','25571','21587'

Pleural effusion:
Tachycardia:

'26716', '7128', '4044', '6503', '4940', '1297', '23647', '51845', '29491', '35124', '3418', '7794', '25266',
'60047', '70366', '1381', '2212', '1664', '1757', '1268', '35127', '96277', '96076', '107472', '23437', '4374',
'4827', '2553', '5484', '41916'

Cheyne-Stokes:

'21042', '27400'

Hepatosplenomegaly:

'3034', '5698', '42038', '9301'

Ascites:

'16113', '54878', '98986', '73305', '52838', '58736', '1508', '29009', '37930'

Cold peripheries:

'17210', '15980', '7213', '16952', '36430'

Oliguria:

'57132', '16063', '30686', '67395'

Confusion:

'3991', '66271', '98746', '100133', '4033', '22466', '41537', '17021', '24077', '22466', '55784', '7389', '5188',
'53446', '52394', '53924'

Depression:

'6546', '6950', '595', '34390', '16506', '15155', '15219', '32159', '43324', '57409', '7011', '15099', '6932',
'35671', '29342', '14709', '25697', '24171', '56273', '55384', '6482', '25563', '3702', '17385', '27491', '9183',
'17770', '1055', '655', '4639', '9055', '18510', '7604', '11177', '9211', '9667', '41989', '22806', '59386', '12099', '24
117', '52678', '24112', '28863', '10667', '98346', '98252', '98414', '98417', '101054', '101153', '103677',

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Palpitations:

'2975', '29469', '16170', '326', '15616', '4789', '15998'

Dizziness:

'5800', '5816', '5820', '6410', '1512', '7417', '6262', '23332', '18564', '15909', '132', '392', '4291', '1114', '393', '15493'

Syncope:

'7431', '11859', '6201', '7279', '6186', '15317', '16267', '2307', '2357', '184', '1405', '1812', '7431'

Raised Jugular venous pressure:

'15900', '10212', '103509'

Edit heart sound:

'57385', '32363', '26669'

Displaced apex pulse:

'64242', '54541'
One-sentence summary

Heart failure patients with high readmission rates have high use of other healthcare services, are associated with poor outcomes, and undergo a repeated cycle of similar causes of hospital admissions compared with the rest of the patient population.

Take-home figure

*Figure 2. Trajectory of mean out-of-hours GP visits in comparison to mean annual readmission rate among subgroups in HF.*
### Characteristics of high-impact users

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Low-impact N [%]</th>
<th>Group 4 (chronic high-impact) N [%]</th>
<th>OR CI (95%)</th>
<th>P value</th>
<th>Group 5 (short-term high-impact) N [%]</th>
<th>OR CI (95%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 75</td>
<td>184 [43.9]</td>
<td>673 [70.8]</td>
<td>1.58 [1.40-1.79]</td>
<td>&lt; 0.001</td>
<td>3555 [69.2]</td>
<td>2.03 [1.82-2.27]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>173 [41.3]</td>
<td>751 [79.1]</td>
<td>13.74 [3.67-51.42]</td>
<td>0.05</td>
<td>2417 [47.1]</td>
<td>1.48 [0.47-4.66]</td>
<td>0.73</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>9 [2.1]</td>
<td>572 [60.2]</td>
<td>11.25 [3.90-32.46]</td>
<td>0.02</td>
<td>1490 [29.0]</td>
<td>3.03 [1.05-8.76]</td>
<td>0.29</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>56 [13.4]</td>
<td>508 [53.5]</td>
<td>5.42 [3.97-7.39]</td>
<td>&lt; 0.001</td>
<td>1310 [25.5]</td>
<td>1.77 [1.31-2.38]</td>
<td>0.05</td>
</tr>
<tr>
<td>Myocarditis/Cardiomyopathy</td>
<td>19 [4.5]</td>
<td>44 [4.6]</td>
<td>0.93 [0.52-1.68]</td>
<td>0.91</td>
<td>273 [5.3]</td>
<td>0.76 [0.43-1.34]</td>
<td>0.61</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>53 [12.6]</td>
<td>318 [33.5]</td>
<td>1.17 [0.86-1.60]</td>
<td>0.61</td>
<td>901 [17.5]</td>
<td>0.68 [0.50-0.91]</td>
<td>0.19</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>17 [4.1]</td>
<td>148 [15.6]</td>
<td>1.15 [0.70-1.90]</td>
<td>0.77</td>
<td>393 [7.6]</td>
<td>0.82 [0.50-1.34]</td>
<td>0.68</td>
</tr>
<tr>
<td>Hypertension</td>
<td>199 [47.5]</td>
<td>869 [91.5]</td>
<td>5.81 [4.44-7.61]</td>
<td>&lt; 0.001</td>
<td>3373 [65.6]</td>
<td>1.79 [1.43-2.23]</td>
<td>0.009</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>177 [42.2]</td>
<td>755 [79.5]</td>
<td>7.17 [1.88-27.99]</td>
<td>0.14</td>
<td>2563 [49.9]</td>
<td>0.52 [0.16-1.68]</td>
<td>0.58</td>
</tr>
<tr>
<td>Diabetes</td>
<td>65 [16.5]</td>
<td>347 [36.5]</td>
<td>2.08 [1.55-2.77]</td>
<td>0.01</td>
<td>1049 [20.4]</td>
<td>1.31 [0.99-1.73]</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Table 1. Sociodemographic and past medical history associated with high-impact users compared with the low-impact users.
<table>
<thead>
<tr>
<th>Condition</th>
<th>High Impact Users</th>
<th>Low Impact Users</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy alcohol intake</td>
<td>88 [21.0]</td>
<td>163 [17.2]</td>
<td>1.32 [1.00-1.75]</td>
<td>0.32</td>
<td>997 [19.4]</td>
</tr>
<tr>
<td>Obesity</td>
<td>57 [13.6]</td>
<td>111 [11.7]</td>
<td>0.80 [0.57-1.14]</td>
<td>0.53</td>
<td>414 [8.1]</td>
</tr>
<tr>
<td>Dementia</td>
<td>1 [0.2]</td>
<td>286 [30.1]</td>
<td>35.16 [8.94-138.38]</td>
<td><strong>0.009</strong></td>
<td>649 [12.6]</td>
</tr>
<tr>
<td>Anaemia</td>
<td>22 [5.2]</td>
<td>499 [52.5]</td>
<td>10.38 [6.82-15.80]</td>
<td><strong>&lt; 0.001</strong></td>
<td>1096 [21.3]</td>
</tr>
<tr>
<td>Renal failure</td>
<td>5 [1.2]</td>
<td>518 [54.5]</td>
<td>2.92 [0.74-11.47]</td>
<td>0.43</td>
<td>1374 [26.7]</td>
</tr>
<tr>
<td>Mental health disorder</td>
<td>13 [3.1]</td>
<td>224 [23.6]</td>
<td>6.11 [3.49-10.70]</td>
<td><strong>0.001</strong></td>
<td>397 [7.7]</td>
</tr>
<tr>
<td>Relationship problems</td>
<td>22 [5.2]</td>
<td>35 [3.7]</td>
<td>1.30 [0.76-2.23]</td>
<td>0.63</td>
<td>250 [4.9]</td>
</tr>
<tr>
<td>Bereavement episodes</td>
<td>48 [11.5]</td>
<td>114 [12.0]</td>
<td>0.52 [0.36-0.75]</td>
<td>0.07</td>
<td>473 [9.2]</td>
</tr>
<tr>
<td>History of smoking</td>
<td>183 [43.7]</td>
<td>359 [37.8]</td>
<td>0.91 [0.79-1.06]</td>
<td>0.52</td>
<td>2305 [44.9]</td>
</tr>
<tr>
<td>Female sex</td>
<td>193 [46.1]</td>
<td>518 [54.5]</td>
<td>0.98 [0.77-1.25]</td>
<td>0.92</td>
<td>2674 [52.1]</td>
</tr>
</tbody>
</table>

**Table 1. Sociodemographic and past medical history associated with high-impact users compared with the low-impact users.**
Management factors related to high-impact users

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Low-impact N [%]</th>
<th>Chronic high-impact N [%]</th>
<th>OR CI (95%)</th>
<th>P value</th>
<th>Short-term high-impact N [%]</th>
<th>OR CI (95%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal function recorded at GP visit</td>
<td>33 [7.9]</td>
<td>672 [70.7]</td>
<td>7.46 [5.00-11.13]</td>
<td>&lt; 0.001</td>
<td>3684 [71.7]</td>
<td>7.17 [4.90-10.49]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>History of flu vaccination</td>
<td>306 [73.0]</td>
<td>264 [27.8]</td>
<td>0.43 [0.33-0.57]</td>
<td>0.002</td>
<td>1328 [25.9]</td>
<td>0.39 [0.30-0.51]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Exercise recommendation by GP</td>
<td>251 [59.9]</td>
<td>440 [46.3]</td>
<td>0.68 [0.54-0.87]</td>
<td>0.12</td>
<td>2505 [48.8]</td>
<td>0.65 [0.52-0.81]</td>
<td>0.05</td>
</tr>
<tr>
<td>Prescribed for medications for suggestive symptoms and signs of heart failure prior to diagnosis</td>
<td>289 [68.9]</td>
<td>618 [65.1]</td>
<td>0.47 [0.34-0.64]</td>
<td>0.01</td>
<td>3225 [62.8]</td>
<td>0.54 [0.41-0.73]</td>
<td>0.03</td>
</tr>
<tr>
<td>3 or more readmissions (vs. &lt;= 2) in the year preceding diagnosis of HF</td>
<td>16 [3.8]</td>
<td>193 [20.3]</td>
<td>1.15 [0.64-2.05]</td>
<td>0.81</td>
<td>415 [8.1]</td>
<td>0.87 [0.49-1.54]</td>
<td>0.79</td>
</tr>
<tr>
<td>Number of consultations by GP in preceding year (4th percentile)</td>
<td>76 [18.1]</td>
<td>272 [28.6]</td>
<td>1.02 [0.90-1.15]</td>
<td>0.87</td>
<td>1022 [19.9]</td>
<td>1.01 [0.90-1.13]</td>
<td>0.93</td>
</tr>
<tr>
<td>Number of patients with increased out of hours’ visits at primary care in preceding year (75th percentile and above for number of visits)</td>
<td>14 [3.3]</td>
<td>78 [8.2]</td>
<td>1.14 [0.95-1.36]</td>
<td>0.46</td>
<td>325 [6.3]</td>
<td>1.14 [0.96-1.35]</td>
<td>0.45</td>
</tr>
<tr>
<td>Patients presenting with atypical signs and</td>
<td>237 [56.6]</td>
<td>622 [65.5]</td>
<td>1.19 [0.92-1.52]</td>
<td>0.49</td>
<td>3037 [59.1]</td>
<td>1.10 [0.87-1.39]</td>
<td>0.67</td>
</tr>
<tr>
<td>Symptoms</td>
<td>High Impact Users</td>
<td>Low Impact Users</td>
<td>p Value</td>
<td>Odds Ratio</td>
<td>95% CI</td>
<td>Odds Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>---------------------------------------</td>
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</tr>
<tr>
<td>HF diagnosed as an inpatient</td>
<td>6 [1.4]</td>
<td>794 [83.6]</td>
<td>&lt; 0.001</td>
<td>42.52 [22.20-81.45]</td>
<td>4312 [83.9]</td>
<td>45.60 [24.29-85.63]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Blood pressure recorded at GP visit</td>
<td>393 [93.8]</td>
<td>793 [83.4]</td>
<td>0.17</td>
<td>0.52 [0.32-0.84]</td>
<td>4794 [93.3]</td>
<td>0.96 [0.61-1.51]</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Table 2. Management related factors associated with high-impact users compared with the low-impact users.
Table 3. The number of episodes of healthcare use and social events in the subgroups during the follow-up period. (The cardiac imaging included chest x-ray, echocardiogram, cardiac angiogram, computed tomography and magnetic resonance imaging of the heart).

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Bereavement (n [per visits]) (p &lt; 0.01)</th>
<th>GP visit for relationship difficulties (n [% per visits]) (p=0.05)</th>
<th>GP out-of-hours visits (n [% per visits]) (p &lt; 0.01)</th>
<th>Visits for HF medication review (n [% per visits]) (p &lt; 0.01)</th>
<th>GP visits for monitoring of blood pressure and renal function (n [% per visits]) (p &lt; 0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 5 (chronic high-impact)</td>
<td>6 [2.6%]</td>
<td>4 [1.7%]</td>
<td>2223 [1.1%]</td>
<td>20010 [9.4%]</td>
<td>3763 [1.8%]</td>
</tr>
<tr>
<td>Group 4 (short-term high-impact)</td>
<td>1 [0.4%]</td>
<td>2 [0.8%]</td>
<td>1217 [1.5%]</td>
<td>7450 [9.1%]</td>
<td>1536 [1.9%]</td>
</tr>
<tr>
<td>Group 3 (intermediate use)</td>
<td>32 [2.5%]</td>
<td>15 [1.2%]</td>
<td>8926 [1.2%]</td>
<td>84517 [11.1%]</td>
<td>15416 [2.0%]</td>
</tr>
<tr>
<td>Group 2 (intermediate use)</td>
<td>48 [3.6%]</td>
<td>19 [1.4%]</td>
<td>8607 [0.8%]</td>
<td>123000 [11.4%]</td>
<td>23811 [2.2%]</td>
</tr>
<tr>
<td>Low-impact (group 1)</td>
<td>95 [1.3%]</td>
<td>53 [0.7%]</td>
<td>12266 [0.6%]</td>
<td>291942 [14.5%]</td>
<td>46334 [2.3%]</td>
</tr>
</tbody>
</table>
### Common sequences of causes of readmissions

<table>
<thead>
<tr>
<th>Common sub-sequences</th>
<th>Group 1 (Low-impact n [%])</th>
<th>Group 2 (intermediate use n [%])</th>
<th>Group 3 (intermediate use n [%])</th>
<th>Group 4 (Short-term high-impact n [%])</th>
<th>Group 5 (Chronic high-impact n [%])</th>
<th>P value</th>
</tr>
</thead>
</table>

Table 4. Common distinct sequences of causes of emergency admissions associated with various subgroups in the patient population.
Figure 1. Trajectories of subgroups among HF patients (dotted lines represent 95% confidence intervals).

- Group 1 (low-impact, 66.5%)
- Group 2 (intermediate, 14.8%)
- Group 3 (intermediate, 13.0%)
- Group 4 (short-term high-impact, 3.3%)
- Group 5 (chronic high-impact, 2.4%)

Mean readmission rate over time (years)
Figure 2. Trajectory of mean out-of-hours GP visits in comparison to mean annual readmission rate among subgroups in HF.
Figure 3. The sequence of healthcare visits in different subgroups of HF patients in the follow-up period.

Different subgroups among heart failure patients with long-term healthcare visits
Figure 4. The proportion of type of healthcare visits during each consecutive health care use among subgroups of HF patients.